10/804,822

```
=> d his

     (FILE 'HOME' ENTERED AT 14:07:19 ON 15 NOV 2006)

     FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH, LIFESCI' ENTERED AT 14:07:36 ON
     15 NOV 2006
L1         4157 S HUMAN(3A)EMBRYONIC(W)STEM(W)CELL OR HUMAN(W)ES(W)CELL
L2       102056 S (DIFFERENTIAT? OR UNDIFFERENTIAT?)(7A)(MARKER OR GENE)
L3          481 S L1(P)L2
L4        12731 S OCT3 OR OCT4 OR SSEA-4 OR SSEA-3 OR CRIPTO OR GRP OR PODXL OR
L5          136 S L3 AND L4
L6        72739 S CD44 OR CD105 OR ENDOGLIN OR CD106 OR CD90 OR STRO-1 OR VIMEN
L7           12 S L3 AND L6
L8          623 S L1 AND L2
L9           14 S L8 AND L6
L10        7022 S HTERT
L11           7 S L8 AND L10
L12           8 DUP REM L7 (4 DUPLICATES REMOVED)
L13          10 DUP REM L9 (4 DUPLICATES REMOVED)
L14           4 DUP REM L11 (3 DUPLICATES REMOVED)

=> d au ti so pi ab 1-8 l12

L12  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN
IN   Stanton, Lawrence W.; Brandenberger, Ralph; Brunette, Elisa; Gold, Joseph
     D.; Irving, John M.; Mandalam, Ramkumar; Mok, Michael; Powell, Sandra E.
TI   Standardization of growth conditions and marker system for human embryonic
     stem cells intended for use in regenerative medicine
SO   U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of Appl. No. PCT/EP04/002808.
     CODEN: USXXCO
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     ----------          ----   --------    --------------------     --------
PI   US 2006134636        A1    20060622    US 2004-804822           20040319
     US 2003224411        A1    20031204    US 2003-388578           20030313
     US 2004180347        A1    20040916    US 2003-389431           20030313
     WO 2004083406        A2    20040930    WO 2004-US8883           20040313
     WO 2004083406        A3    20050331
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
     WO 2004080146        A2    20040923    WO 2004-EP2808           20040315
     WO 2004080146        A3    20050909
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
AB   This disclosure provides a system for qualifying embryonic stem cells
     intended for human therapy.  A comprehensive sequencing project has
     identified important markers that are characteristic of undifferentiated
```

pluripotent cells. Cripto protein, gastrin-releasing peptide receptor, podocalyxin-like protein, hTERT, and Oct 3/4 protein are used as the markers. Combinations of these markers have been used to screen feeder cells, media additives, and culture conditions that promote rapid expansion of stem cells without differentiation. By measuring undifferentiated stem cell markers, and markers formed by early progenitors such as stromal cells, the user can quantitate the proportion and extent of differentiation. This establishes standardized criteria for master cell banks and cell cultures that can then be used to produce therapeutic cell populations and medicaments for use in regenerative medicine.

L12 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
IN Moore, Harry; Gerskowitch, Paul; Harun, Rosliah
TI Culture of human cytotrophoblast stem cells expressing HLA-G and HLA-I antigens, and use for tissue engineering and drug screening
SO Brit. UK Pat. Appl., 42pp.
CODEN: BAXXDU

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2425129	A1	20061018	GB 2006-6875	20060406

AB Cytotrophoblast stem cells which express HLA-G and HLA class I antigens have been isolated. Preferably, human cytotrophoblast stem cells are derived from human embryonic stem cells, by culturing embryoid bodies and enriching for embryoid bodies expressing high levels of chorionic gonadotrophin. Human cytotrophoblast stem cells may also be isolated by enriching for cytotrophoblast stem cells that express HLA-G and HLA class I antigen. The isolated cytotrophoblast stem cells may be used for tissue engineering, the modulation of tissue rejection in transplantation therapy, the identification of genes associated with cytotrophoblast stem cell differentiation, the preparation of a library of cytotrophoblast stem cell specific gene products, methods of screening agents that modulate the angiogenic effects of endothelial cells, and the production of mixed cell compns. or chimeric cells.

L12 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
IN Schulz, Thomas C.; Condie, Brian G.; Davidson, Bruce; Stice, Steven L.
TI Neural differentiation of human pluripotent embryonic stem cells using serum free MEDII conditioned medium and use for neural disease treatment
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004015077	A2	20040219	WO 2003-US24864	20030808
WO 2004015077	A3	20040513		
WO 2004015077	C2	20040617		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2003095629	A1	20031120	WO 2003-AU552	20030509

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003259072 A1 20040225 AU 2003-259072 20030808

EP 1534068 A2 20050601 EP 2003-785049 20030808

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 2006121607 A1 20060608 US 2005-524157 20050822

AB The present invention provides compns. and methods for human neural cell production More particularly, the present invention provides cellular differentiation methods employing an essentially serum free MEDII conditioned medium, together with SSEA4 selection and protease passaging techniques for the generation of human neural cells from pluripotent and multipotent human stem cells. Formation and characterization of embryoid bodies from human embryonic stem cells in serum-free conditions is shown. The invention provides a method of treating a patient with a neural disease by administering a therapeutically effective amount of the neural cells produced using the methods of the invention.

L12 ANSWER 4 OF 8 MEDLINE on STN DUPLICATE 1

AU Ginis Irene; Luo Yongquan; Miura Takumi; Thies Scott; Brandenberger Ralph; Gerecht-Nir Sharon; Amit Michal; Hoke Ahmet; Carpenter Melissa K; Itskovitz-Eldor Joseph; Rao Mahendra S

TI Differences between human and mouse embryonic stem cells.

SO Developmental biology, (2004 May 15) Vol. 269, No. 2, pp. 360-80. Journal code: 0372762. ISSN: 0012-1606.

AB We compared gene expression profiles of mouse and human ES cells by immunocytochemistry, RT-PCR, and membrane-based focused cDNA array analysis. Several markers that in concert could distinguish undifferentiated ES cells from their differentiated progeny were identified. These included known markers such as SSEA antigens, OCT3/4, SOX-2, REX-1 and TERT, as well as additional markers such as UTF-1, TRF1, TRF2, connexin43, and connexin45, FGFR-4, ABCG-2, and Glut-1. A set of negative markers that confirm the absence of differentiation was also developed. These include genes characteristic of trophoectoderm, markers of germ layers, and of more specialized progenitor cells. While the expression of many of the markers was similar in mouse and human cells, significant differences were found in the expression of vimentin, beta-III tubulin, alpha-fetoprotein, eomesodermin, HEB, ARNT, and FoxD3 as well as in the expression of the LIF receptor complex LIFR/IL6ST (gp130). Profound differences in cell cycle regulation, control of apoptosis, and cytokine expression were uncovered using focused microarrays. The profile of gene expression observed in H1 cells was similar to that of two other human ES cell lines tested (line I-6 and clonal line-H9.2) and to feeder-free subclones of H1, H7, and H9, indicating that the observed differences between human and mouse ES cells were species-specific rather than arising from differences in culture conditions.

L12 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

AU Mayer-Proschel, Margot; Liu, Ying; Xue, Haipeng; Wu, Yuanyuan; Carpenter, Melissa K.; Rao, Mahendra S.

TI Human neural precursor cells - an in vitro characterization

SO Clinical Neuroscience Research (2002), 2(1-2), 58-69 CODEN: CNRLBU; ISSN: 1566-2772

AB We have compared the properties of human neural precursors isolated from fetal tissue with progenitor and precursor cells identified from rodent fetal tissue and human excretory/secretory (ES) cells. We have identified multipotent human neuroepithelial precursor cells (hNEPs) that are fibroblast growth factor dependent, grow in adherent culture, and differentiate into neurons, astrocytes, and oligodendrocytes in mass and clonal cultures. A subset of these multipotent cells express an antigen

recognized by the AC133/2 antibody. HNEPs appear similar to rodent-derived NEP cells, and unlike other human multipotent precursor cell populations, do not require Leukemia Inhibitory Factor (LIF) or Epithelial Growth Factor (EGF) for their survival. HNEPs constitute a small fraction of the cells present at any stage examined and three addnl. dividing populations can be identified based on expression of epitopes recognized by E-NCAM, A2B5 and CD44. E-NCAM+ cells co-express neuronal markers and can differentiate into multiple classes of neurons. Two types of A2B5+ cells can be distinguished: a small neuronal population that co-expresses E-NCAM immunoreactivity and a larger glial population that is E-NCAM neg. CD44+ cells do not express neuronal markers or oligodendrocytic markers but co-express astrocytic markers and likely represent an astrocyte precursor cell. Dividing E-NCAM+, A2B5+ and CD44+ cells can be identified in differentiating human ES cell cultures and the properties of these cells appear similar to cells present in fetal tissue.

L12 ANSWER 6 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AU Cheng, Linzhao [Reprint Author]; Hammond, Holly [Reprint Author]; Ye, Zhaohui [Reprint Author]; Zhan, Xiangcan [Reprint Author]; Dravid, Gautam [Reprint Author]

TI Adult Human Marrow Cells Support Prolonged Expansion of Undifferentiated Human Embryonic Stem Cells.

SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 504. print. Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

AB Human embryonic stem (ES) cell lines provide unprecedented opportunities to study self-renewal and differentiation of embryonic and adult stem cells, and to develop novel cell-based therapies. It was reported that primary mouse embryonic fibroblasts (MEFs) were required as feeder cells until recently to support prolonged growth of human ES cells. Unlike mouse ES cells, adding growth factors such as LIF in the absence of MEFs is insufficient to maintain undifferentiated human ES cells. It is unclear about the nature of factors made by MEFs. Contrary to a previous report from Geron(1), we and others could not achieve prolonged growth of undifferentiated human ES cells using the MEF conditioned medium together with Laminin or Matrigel (ECM extracts from mouse sarcoma)(2). The presence of rodent cells or uncharacterized animal proteins in the current culture systems imposes a risk to clinical uses of human ES cells. While others looked for an MEF replacement with human fetal cells and primary adult oviduct cells(2), we attempted to use easily accessible human adult cells such as marrow stromal cells (MSCs). We used an improved method to derive and expand human MSCs efficiently and consistently from adult bone marrow (BM) aspirates. After a primary and 2 subsequent passages in culture (in less than 6 weeks), 75-200 million MSCs (p2) can be obtained from a 10cc BM sample. These culture-expanded cells displayed characteristics associated with BM-derived mesenchymal stem cells as previously described. The MSCs of p2 to p5 from multiple donors were used to support the growth of the H1 human ES cell line under a serum-free culture condition; all giving similar results. Undifferentiated ES colonies cultured on MSC feeders (irradiated and mitotically inactive) amplified more than 100 fold during the 30 day continuous culture (5 passages), similar to or better than what was reported with the H1 ES cells cultured on MEFs. The amplified ES colonies retained unique morphology and molecular markers, characteristic of undifferentiated human ES cells as cultured on MEFs. They express the Oct-4 transcription factor, a membrane alkaline phosphatase and SSEA-4, but not SSEA-1 or SH-2/CD105 (a marker for MSCs). Preliminary data suggest that the MSC-ES cell contact is important to the

optimal growth of undifferentiated human ES cells. We are currently investigating whether human ES cells cultured on MSCs may gain advantages in subsequent BM engraftment and/or hematopoiesis upon differentiation. The well-studied MSCs and the defined cell culture system (animal cell-free and serum-free) may provide a clinically and ethically feasible method to expand human ES cells for novel cell therapies. In addition, it is of great interest to identify factors that are made by human MSCs to support the self-newal of human ES and adult stem cells. (1) Xu, et al. Nature Biotech. 19: 971 (2001); (2) Richards, et al. Nature Biotech. August/September 2002.

L12 ANSWER 7 OF 8 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AU Zhan, Xiangcan [Reprint Author]; Dravid, Gautam [Reprint Author]; Hammond, Holly [Reprint Author]; Ye, Zhaohui [Reprint Author]; Yang, Xiaoming [Reprint Author]; Cheng, Linzhao [Reprint Author]
TI Lympho-Hematopoiesis from Differentiated Human Embryonic Stem (ES) Cells.
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 1121. print. Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
AB Human embryonic stem (ES) cell lines provide unprecedented opportunities to study self-renewal and differentiation of embryonic and adult stem cells. Emerging data suggest that human ES cells are distinct from mouse counterparts in many critical properties. Therefore, it is necessary to study directly human ES cells and their differentiation, including lympho-hematopoiesis. Kaufman et al. reported (PNAS, 2001) that apprx5% CD34+ cells can be generated from human ES cells, upon differentiation on stromal cells. Erythorid-myeloid colony forming cells (CFCs) were found (up to 0.04%) and so were fewer megakaryocytic progenitors. However, production of lymphopoietic and other hematopoietic lineages has not been reported. We also used the H1 ES line (from WiCell) and attempted to generate broader ranges of lympho-hematopoietic cells including B cells and other antigen-presenting cells (APCs). Undifferentiated human ES cells express surface markers such as SSEA-4, CD90 and CD133, but lack CD45, CD31; CD34, CD41, CD14, CD19, CD16 or MHC class II. The H1 ES cells were forced to differentiation in suspension culture as embryoid bodies (EBs). Under the best of various conditions tested, 80% of EBs became cystic within 10 days. EBs were then placed under hematopoietic differentiation conditions with or without stromal cells. When cultured on OP9 stromal cells with early-acting cytokines, cells resembling primitive hematopoietic cells emerged after 3 days and continued proliferating as blast cell clusters. Suspension cells were harvested starting at day 8 and analyzed by FACS. We found the differentiated suspension cells acquired various hematopoietic markers such as CD45, CD31, CD34, and CD41 (76%, 61%, 14%, and 56.5%, respectively). When assayed in methylcellulose for CFCs, we found that 0.15% of the suspension cells formed CFC-GM, greater than cord blood mononuclear cells (0.08%). CD19+ (pro-B) cells were also detected (5.6%) at day 8. Similar results were obtained with the suspension cells emerged from outgrowing whole EBs (undigested and plastic adherent) in the absence of OP9 cells. We continued harvesting hematopoietic CFCs (up to 0.23% of the cells in suspension) and other CD45+ cells in the following weeks. In addition to B cells and myeloid (CD33+ and CD14+) cells, we also found CD2+CD16+ and CD16+CD56+ NK cells, but not CD3+ T cells. When EB-derived cells were cultured with GM-CSF, IL-4 in order to stimulate APC production, we found that up to 33% cells expressed MHC class II and more than 50% cells expressed CD80 or CD86, co-stimulatory molecules required for antigen presentation and T cell activation. The MHC class II+ cells include B cells, macrophages and dendritic cells, and play a central role in (T cell) immune responses. The differentiated hematopoietic cells

comprising MHC class II+ cells indeed elicited allogeneic human T cell responses in MLR assays, particularly after activation by TNFa. This study demonstrated that differentiated human ES cells can generate large numbers of lympho-hematopoietic cells, including functional APCs, over an extended time period. Therefore, human ES cell lines will provide a powerful system to study early events of human lympho-hematopoiesis, and to develop novel cell-based therapies that require reconstituting or reprogramming patient's blood/immune systems.

L12 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
IN Pera, Martin Frederick; Ben-Hur, Tamir
TI Embryonic stem cells and neural progenitor cells derived therefrom
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001068815	A1	20010920	WO 2001-AU278	20010314
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2403000	AA	20010920	CA 2001-2403000	20010314
AU 2001040361	A5	20010924	AU 2001-40361	20010314
AU 779694	B2	20050203		
EP 1263932	A1	20021211	EP 2001-911277	20010314
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004500103	T2	20040108	JP 2001-567299	20010314
AU 2005200148	A1	20050210	AU 2005-200148	20050113

AB The present invention relates to undifferentiated human embryonic stem cells, methods of cultivation and propagation and production of differentiated cells. In particular it relates to the production of human ES cells capable of yielding somatic differentiated cells in vitro, as well as committed progenitor cells such as neural progenitor cells capable of giving rise to mature somatic cells including neural cells and/or glial cells and uses thereof. In one aspect of the present invention, there is provided an enriched preparation of undifferentiated human embryonic stem cells capable of proliferation in vitro and differentiation to neural progenitor cells, neuron cells and/or glial cells. This invention provides a method that generates an in vitro and in vivo model of controlled differentiation of ES cells towards the neural lineage. The model, and the cells that are generated along the pathway of neural differentiation may be used for the study of the cellular and mol. biol. of human neural development, for the discovery of genes, growth factors, and differentiation factors that play a role in neural differentiation and regeneration, for drug discovery and for the development of screening assays for teratogenic, toxic and neuroprotective effects.

=> d au ti so pi 1-10 l13

L13 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
IN Stanton, Lawrence W.; Brandenberger, Ralph; Brunette, Elisa; Gold, Joseph D.; Irving, John M.; Mandalam, Ramkumar; Mok, Michael; Powell, Sandra E.
TI Standardization of growth conditions and marker system for human embryonic stem cells intended for use in

regenerative medicine
SO U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of Appl. No. PCT/EP04/002808.
CODEN: USXXCO

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006134636	A1	20060622	US 2004-804822	20040319
US 2003224411	A1	20031204	US 2003-388578	20030313
US 2004180347	A1	20040916	US 2003-389431	20030313
WO 2004083406	A2	20040930	WO 2004-US8883	20040313
WO 2004083406	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004080146	A2	20040923	WO 2004-EP2808	20040315
WO 2004080146	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

L13 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
IN Moore, Harry; Gerskowitch, Paul; Harun, Rosliah
TI Culture of human cytotrophoblast stem cells expressing HLA-G and HLA-I antigens, and use for tissue engineering and drug screening
SO Brit. UK Pat. Appl., 42pp.
CODEN: BAXXDU

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2425129	A1	20061018	GB 2006-6875	20060406

L13 ANSWER 3 OF 10 MEDLINE on STN
AU Park Chang-Hwan; Minn Yang-Ki; Lee Ji-Yeon; Choi Dong Ho; Chang Mi-Yoon; Shim Jae-Won; Ko Ji-Yun; Koh Hyun-Chul; Kang Min Jeong; Kang Jin Sun; Rhie Duck-Joo; Lee Yong-Sung; Son Hyeon; Moon Shin Yong; Kim Kwang-Soo; Lee Sang-Hun
TI In vitro and in vivo analyses of human embryonic stem cell-derived dopamine neurons.
SO Journal of neurochemistry, (2005 Mar) Vol. 92, No. 5, pp. 1265-76.
Journal code: 2985190R. ISSN: 0022-3042.

L13 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
IN Schulz, Thomas C.; Condie, Brian G.; Davidson, Bruce; Stice, Steven L.
TI Neural differentiation of human pluripotent embryonic stem cells using serum free MEDII conditioned medium and use for neural disease treatment
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2004015077 A2 20040219 WO 2003-US24864 20030808
WO 2004015077 A3 20040513
WO 2004015077 C2 20040617
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2003095629 A1 20031120 WO 2003-AU552 20030509
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003259072 A1 20040225 AU 2003-259072 20030808
EP 1534068 A2 20050601 EP 2003-785049 20030808
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 2006121607 A1 20060608 US 2005-524157 20050822

L13 ANSWER 5 OF 10 MEDLINE on STN DUPLICATE 1
AU Ginis Irene; Luo Yongquan; Miura Takumi; Thies Scott; Brandenberger Ralph; Gerecht-Nir Sharon; Amit Michal; Hoke Ahmet; Carpenter Melissa K; Itskovitz-Eldor Joseph; Rao Mahendra S
TI Differences between human and mouse embryonic stem cells.
SO Developmental biology, (2004 May 15) Vol. 269, No. 2, pp. 360-80. Journal code: 0372762. ISSN: 0012-1606.

L13 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
IN Pera, Martin Frederick; Laslett, Andrew; Hawes, Susan; Gion, Tomonobu
TI Characterization and isolation of subsets of human embryonic stem cells (HES) using GCTM-2 antigen as a marker
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003040355	A1	20030515	WO 2002-AU1534	20021111

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2466342	AA	20030515	CA 2002-2466342	20021111
GB 2398079	A1	20040811	GB 2004-12528	20021111
GB 2398079	B2	20060531		
EP 1448763	A1	20040825	EP 2002-774172	20021111

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

GB 2419890	A1	20060510	GB 2006-2441	20021111
US 2005095708	A1	20050505	US 2004-841907	20040507

L13 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
AU Mayer-Proschel, Margot; Liu, Ying; Xue, Haipeng; Wu, Yuanyuan; Carpenter, Melissa K.; Rao, Mahendra S.
TI Human neural precursor cells - an in vitro characterization
SO Clinical Neuroscience Research (2002), 2(1-2), 58-69
CODEN: CNRLBU; ISSN: 1566-2772

L13 ANSWER 8 OF 10 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AU Cheng, Linzhao [Reprint Author]; Hammond, Holly [Reprint Author]; Ye, Zhaohui [Reprint Author]; Zhan, Xiangcan [Reprint Author]; Dravid, Gautam [Reprint Author]
TI Adult Human Marrow Cells Support Prolonged Expansion of Undifferentiated Human Embryonic Stem Cells.
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 504. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

L13 ANSWER 9 OF 10 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
AU Zhan, Xiangcan [Reprint Author]; Dravid, Gautam [Reprint Author]; Hammond, Holly [Reprint Author]; Ye, Zhaohui [Reprint Author]; Yang, Xiaoming [Reprint Author]; Cheng, Linzhao [Reprint Author]
TI Lympho-Hematopoiesis from Differentiated Human Embryonic Stem (ES) Cells.
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 1121. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

L13 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
IN Pera, Martin Frederick; Ben-Hur, Tamir
TI Embryonic stem cells and neural progenitor cells derived therefrom
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001068815	A1	20010920	WO 2001-AU278	20010314
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2403000	AA	20010920	CA 2001-2403000	20010314
AU 2001040361	A5	20010924	AU 2001-40361	20010314
AU 779694	B2	20050203		
EP 1263932	A1	20021211	EP 2001-911277	20010314
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004500103	T2	20040108	JP 2001-567299	20010314
AU 2005200148	A1	20050210	AU 2005-200148	20050113

=> d au ti so pi ab 1-4 l14

L14 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

IN Stanton, Lawrence W.; Brandenberger, Ralph; Brunette, Elisa; Gold, Joseph D.; Irving, John M.; Mandalam, Ramkumar; Mok, Michael; Powell, Sandra E.

TI Standardization of growth conditions and marker system for human embryonic stem cells intended for use in regenerative medicine

SO U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of Appl. No. PCT/EP04/002808.
CODEN: USXXCO

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006134636	A1	20060622	US 2004-804822	20040319
US 2003224411	A1	20031204	US 2003-388578	20030313
US 2004180347	A1	20040916	US 2003-389431	20030313
WO 2004083406	A2	20040930	WO 2004-US8883	20040313
WO 2004083406	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004080146	A2	20040923	WO 2004-EP2808	20040315
WO 2004080146	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

AB This disclosure provides a system for qualifying embryonic stem cells intended for human therapy. A comprehensive sequencing project has identified important markers that are characteristic of undifferentiated pluripotent cells. Cripto protein, gastrin-releasing peptide receptor, podocalyxin-like protein, hTERT, and Oct 3/4 protein are used as the markers. Combinations of these markers have been used to screen feeder cells, media additives, and culture conditions that promote rapid expansion of stem cells without differentiation. By measuring undifferentiated stem cell markers, and markers formed by early progenitors such as stromal cells, the user can quantitate the proportion and extent of differentiation. This establishes standardized criteria for master cell banks and cell cultures that can then be used to produce therapeutic cell populations and medicaments for use in regenerative medicine.

L14 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

IN Stanton, Lawrence W.; Brandenberger, Ralph; Gold, Joseph D.; Irving, John M.; Mandalam, Ramkumar; Mok, Michael

TI Marker system for preparing and characterizing high-quality human embryonic stem cells for human therapy

SO U.S. Pat. Appl. Publ., 57 pp.
CODEN: USXXCO

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004180347	A1	20040916	US 2003-389431	20030313
WO 2004080146	A2	20040923	WO 2004-EP2808	20040315

WO 2004080146 A3 20050909
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2006134636 A1 20060622 US 2004-804822 20040319

AB This disclosure provides a system for qualifying embryonic stem cells intended for human therapy. A large-scale sequencing project has identified important markers that are characteristic of undifferentiated pluripotent cells. Cripto protein, gastrin-releasing peptide receptor, podocalyxin-like protein, hTERT, and Oct 3/4 protein are used as the markers. Combinations of these markers can be used to validate the self-renewing capacity of ES cells, and their ability to differentiate into tissue types suitable for regenerative medicine. The marker system of this invention has been used to screen feeder cells, media additives, and culture conditions that promote proliferation of stem cells without differentiation. A culture system optimized by following these markers is suitable for rapid expansion of undifferentiated cells from existing lines, or the derivation of new lines that are equally apposite for clin. use.

L14 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 1

AU Xu Chunhui; Jiang Jianjie; Sottile Virginie; McWhir Jim; Lebkowski Jane; Carpenter Melissa K

TI Immortalized fibroblast-like cells derived from human embryonic stem cells support undifferentiated cell growth.

SO Stem cells (Dayton, Ohio), (2004) Vol. 22, No. 6, pp. 972-80. Journal code: 9304532. ISSN: 1066-5099.

AB Human embryonic stem cells (hESCs) have the potential to generate multiple cell types and hold promise for future therapeutic applications. Although undifferentiated hESCs can proliferate indefinitely, hESC derivatives significantly downregulate telomerase and have limited replication potential. In this study we examine whether the replicative lifespan of hESC derivatives can be extended by ectopic expression of human telomerase reverse transcriptase (hTERT), the catalytic component of the telomerase complex. To this end, we have derived HEF1 cells, a fibroblast-like cell type, differentiated from hESCs. Infection of HEF1 cells with a retrovirus expressing hTERT extends their replicative capacity, resulting in immortal human HEF1-hTERT cells. HEF1-hTERT cells can be used to produce conditioned medium (CM) capable of supporting hESC growth under feeder-free conditions. Cultures maintained in HEF1-CM show characteristics similar to mouse embryonic fibroblast CM control cultures, including morphology, surface marker and transcription factor expression, telomerase activity, differentiation, and karyotypic stability. In addition, HEF1-hTERT cells have the capacity to differentiate into cells of the osteogenic lineage. These results suggest that immortalized cell lines can be generated from hESCs and that cells derived from hESCs can be used to support their own growth, creating a genotypically homogeneous system for the culture of hESCs.

L14 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

AU Tzukerman, Maty; Shachaf, Catherine; Ravel, Yael; Braunstein, Ilana; Cohen-Barak, Orit; Yalon-Hacohen, Michal; Skorecki, Karl L.

TI Identification of a novel transcription factor binding element involved in the regulation by differentiation of the human telomerase (hTERT

) promoter

SO Molecular Biology of the Cell (2000), 11(12), 4381-4391
CODEN: MBCEEV; ISSN: 1059-1524

AB Three different cell differentiation exptl. model systems (human embryonic stem cells, mouse F9 cells, and human HL-60 promyelocytic cells) were used to determine the relationship between the reduction in telomerase activity after differentiation and the regulation of the promoter for the hTERT gene. Promoter constructs of three different lengths were subcloned into the PGL3-basic luciferase reporter vector. In all three exptl. systems, all three promoter constructs drove high levels of reporter activity in the nondifferentiated state, with a marked and time-dependent reduction after the induction of differentiation. In all cases, the smallest core promoter construct (283 nt upstream of the ATG) gave the highest activity. Electrophoretic mobility shift assays revealed transcription factor binding to two E-box domains within the core promoter. There was also a marked time-dependent reduction in this binding with differentiation. In addition, a distinct and novel element was identified within the core promoter, which also underwent time-dependent reduction in transcription factor binding with differentiation. Site-directed mutagenesis of this novel element revealed a correlation between transcription factor binding and promoter activity. Taken together, the results indicate that regulation of overall telomerase activity with differentiation is mediated at least in part at the level of the TERT promoter and provides new information regarding details of the regulatory interactions that are involved in this process.

=>